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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/628,088	07/25/2003	James F. Young	10271-072-999	5542

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EXAMINER	
HORNING, MICHELLE S	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 10/16/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/628,088	YOUNG ET AL.	
	Examiner	Art Unit	
	Michelle Horning	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *34-49 and 85-113* is/are pending in the application.

4a) Of the above claim(s) *93-113* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *34-49 and 85-92* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This office action is responsive to communication filed on 7/26/2006. The status of the claims is as follows: claims 1-33 and 50-84 have been cancelled, claims 34-49 and 85-113 are pending and 34-49 and 85-92 are under current examination.

Applicant's election with traverse of Group III in the reply filed on 7/26/2006 is acknowledged. The traversal is on the ground(s) that rejoining the distinct inventions would not require a serious burden on the examiner because the subject matter is "so intertwined" across the separate groups. Following initial examination, this is not found to be true. In order to search of all of the claims as requested by Applicant, multiple database searches are necessary leading to a serious burden.

The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections

35 U.S.C. 112, 2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 35, 44, 45 and 86 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The above claims are drawn to multiple SEQ ID NO's and, as written, drawn to multiple interpretations. An example is the recitation "SEQ ID NO:390 to 398" of claim 35. It is not clear if claim 35 is drawn to one SEQ ID NO or all of them linked together.

Claim 89 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. As written, it is not clear what the antibodies or antigen-binding fragments are suppose to bind to and it is suggested to insert the word "antigen" after "type 4".

35 U.S.C. 103(a)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 34, 37, 39-42, 45-47, 49, 85 and 90-92 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent Application 09/848,390

(hereinafter "Johnson") in view of Van Den Hoogen et al (2001-cited in IDS) and UniProtKB/TrEMBL entry Q91F55 (2001). The limitations of the claims are as follows:

1. a pharmaceutical composition comprising one or more antibodies immunospecific to an RSV antigen and one or more antibodies immunospecific to an hMPV antigen, more specifically, SEQ ID NO: 420;

2. wherein the RSV antigen is RSV F;

3. wherein at least one of the antibodies cross-react with a turkey APV antigen, more specifically to turkey APV F; and

4. wherein the antibodies neutralize either hMPV, RSV or PIV.

Johnson discloses a combination therapy for multiple respiratory diseases using antibodies (see title and abstract). Johnson specifically teaches a therapeutic composition comprising an anti-RSV neutralizing antibody, including an antibody specific for the F epitope of RSV, or a variant thereof, including active fragments thereof, and an antiviral agent having therapeutic value in the treatment of PIV (see paragraph 16). Johnson also teaches therapeutically effective compositions comprising a monoclonal antibody, including high affinity neutralizing antibodies against PIV in addition to RSV (see paragraph 23). While Johnson teaches compositions for combination therapy using antibodies targeting multiple respiratory diseases, this reference does not disclose treatment of hMPV.

Van Den Hoogen et al were the first to identify and characterized the hMPV in 2001. Van Den Hoogen teaches that this virus has been circulating in the Netherlands for more than 50 years and that nearly all children are exposed to it (see abstract).

Further, entry Q91F55 discloses the hMPV sequence (SEQ ID NO:420) and Van Den Hoogen et al teach that hMPV F is 80% homologous to the translated sequences of APV F and even higher in other protein regions; for example, hMPV M is 87% homologous to APV M (see under RAP-PCR). Given that it is *inherent* for an antibody against one protein to cross-react with a homologous protein, there is an expectation for the cross-reactivity of antibodies between hMPV and APV antigens.

It would have been obvious to one of ordinary skill in the art to modify the methods taught by Johnson and Van Den Hoogen in order to treat multiple respiratory diseases within a single composition, including antibodies that neutralize hMPV. One would have been motivated to so, as disclosed by Van Den Hoogan, because hRSV is the single most important cause of lower respiratory tract infections in children worldwide (see introduction) and hMPV commonly infects children leading to considerable clinical and economical impact (see discussion). There would have been a reasonable expectation of success, given that the underlying protocols in producing antibodies for respiratory viruses are widely used (see Johnson for methods). Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claims 34, 37-42, 48-49, 85-88 and 90-92 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent Application 09/848,390 (hereinafter "Johnson") and further in view of Van Den Hoogen et al (2001), Gazumyan et al (2000), The Impact-RSV Study Group (1998) and Accession # O55887 (1998). In addition to the limitations mentioned above, the limitations to these claims are:

1. a pharmaceutical composition comprising one or more antibodies immunospecific to an RSV antigen and one or more antibodies immunospecific to an hMPV antigen;

2. wherein the hMPV antigen is hMPV F protein;

3. wherein an antibody is Palivizumab (aka Synagis); and

4. wherein an antibody immunospecifically binds to subtype A or B RSV.

The prior art references, Johnson and Van Den Hoogen et al do not disclose the use of Palivizumab or a composition for the treatment of RSV subgroups, A and B. Gazumyan et al discloses that Palivizumab is a monoclonal neutralizing antibody and the only approved drug used for both the prevention and treatment of RSV in high risk patients (see abstract and section 3.1.6). Gazumyan et al further discloses that RSV shows comparatively little antigenic variation and the 2 only subgroups, A and B, are stable antigenically (see section 3.1.6). Of note, The Impact-RSV Study Group discloses that Palivizumab binds to the F-protein of RSV and is active against both type A and B RSV isolates (see introduction). Thus, it would have been obvious for one of ordinary skill in the art to modify the methods taught by Johnson and Van Den Hoogen and further incorporate the antibody that binds either subgroup A or B like Palivizumab as taught by Gazumyan et al. One would have been motivated to do so, as disclosed by Gazumyan et al, because the only successful therapy for RSV is passive immunization via a neutralizing antibody and administration of Palivizumab achieves the best results (see section 3.1.6). There would have been a reasonable expectation of success, given the success of Palivizumab administration for the treatment of RSV subgroups A and B.

Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

The Johnson reference does not disclose a composition for the treatment of hMPV or PIV (via antibodies to SEQ ID NO: 415). Van Den Hoogen et al describes the hMPV virus as well as provides sequence homology alignments for the hMPV-F protein with that of other paramyxoviruses. Van Den Hoogen et al does not disclose making an antibody against the hMPV-F antigen; however, it is well known in the prior art that the F proteins in paramyxoviruses including PIV play an important therapeutic target and this is taught by Gazumyan et al. Section 2 of this reference teaches that both the F and G proteins are functionally similar across paramyxoviruses. Further, the surface glycoprotein F appears to be one of the major immunogenic proteins and facilitates fusion with the target cell membrane. The fusion protein of PIV set forth as SEQ ID NO: 415 is known in the prior art and is disclosed as Accession # O55887. It would have been obvious to one of ordinary skill in the art to modify the method taught by Johnson to further incorporate antibodies that bind to the F region of hMPV or PIV. One would have been motivated to do so, as suggested by Gazumyan et al, since the F glycoprotein has been identified as one of the major virus-neutralizing antigen during viral replication (3.1.4). There would have reasonable expectation of success, given the knowledge that other antibodies, such as Palivizumab, has achieved much success by target binding to the F region in the treatment of other paramyxoviruses. Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claims 34-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent Application 09/848,390 (hereinafter "Johnson"), Van Den Hoogen et al (2001), Gazumyan et al (2000), The Impact-RSV Study Group (1998) and Accession # O55887 (1998) and further in view of WO96/40945 (hereinafter "Li et al"). Claim 34 from which claim 35 and 36 depend is rejected as applied above under 35 U.S.C. 103(a). The limitations of claim 35 and 36 are a pharmaceutical composition comprising at least one antibody that binds to an hMPV antigen and at least one that binds to an RSV antigen as set forth by SEQ ID NO: 391 or at least 90% thereof. Li et al and many other prior art references teach the RSV-F antigen at varying percentages of homology to SEQ ID NO:391 and lengths of sequence; however, no prior art reference discloses a 100% match to the sequence set forth in SEQ ID NO: 391. As only a single example of the prior art references, Li et al disclose an RSV-F antigen in which 240 contiguous amino acids align 100% to the 574 amino acids in SEQ ID NO: 391 (see Example 1, Figure 3). Also, this prior reference teaches the generation of antibodies against the truncated forms of RSV-F (transmembrane spanning regions truncated out) for vaccines (see Abstract). While the instant specification fails to specifically disclose an epitope in the RSV-F antigen to which the antibody would bind, Li et al claim antibodies against the RSV-F sequence mentioned above including the 240 amino acids that are homologous to SEQ ID NO:391 of the instant application. Given that the limitations of claim 34 are met with the prior art references mentioned above, including Gazumyan et al and Johnson and Van Den Hoogen, and that it is an *inherent* property

for an antibody to bind to two proteins sharing homologous sequences or common binding sites, these claims are rejected.

Claims 34, 40 and 43-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent Application 09/848,390 (hereinafter "Johnson"), Van Den Hoogen et al (2001), Gazumyan et al (2000), The Impact-RSV Study Group (1998) and Accession # O55887 (1998) and further in view of Seal et al (2000). Claims 34 and 40 from which claims 43-44 depend are rejected as applied above under 35 U.S.C. 103(a). The limitations of claims 43-44 are a pharmaceutical composition comprising at least one antibody that binds to an hMPV antigen and at least one antibody that binds to an RSV antigen wherein at least one antibody cross-reacts with a turkey APV antigen from subtypes A, B and C, more specifically, the sequence set forth by SEQ ID NO:424. Seal et al disclose that the F protein of APV subtype C is 72% and 71% homologous to the F protein of APV subtype A and APV subtype B, respectively (see Abstract). Further, Van Den Hoogen et al teach that hMPV F is 80% homologous to the translated sequences of APV F (see under RAP-PCR). Given that the limitations of claims 34 and 40 are met with the prior art references mentioned above, including Gazumyan et al and Johnson and Van Den Hoogen, and that it is an *inherent* property for an antibody to bind to proteins sharing homologous sequences, these claims are rejected.

Claims 34, 85 and 89 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent Application 09/848,390 (hereinafter "Johnson"), Van Den Hoogen et al (2001), Gazumyan et al (2000), The Impact-RSV Study Group

(1998), Accession # O55887 (1998) and further in view of Vainionpaa and Hyypia (1994). Claims 34 and 85 from which claim 89 depends are rejected as applied above under 35 U.S.C. 103(a). The limitations of the above claims are a pharmaceutical composition comprising at least one antibody that immunospecifically binds to an RSV antigen, at least one that immunospecifically binds to an hMPV antigen and at least one antibody that immunospecifically binds a PIV antigen including PIV types 1, 2, 3 or 4. The combined prior art references used to reject claims 34 and 85 above do not disclose antibodies that bind to a PIV antigen, including PIV types 1-4. Vainionpaa and Hyypia teach that both prevention and treatment of PIVs is important because this virus is a significant cause of morbidity, especially in infants and young children (see Prevention and Treatment). One would have been motivated to incorporate antibodies that bind to PIV antigens of types 1-4 into the pharmaceutical composition because, as suggested by Vainionpaa and Hyypia, "Parainfluenza viruses 1 through 4 (PIV1 through PIV4) are important human pathogens that cause upper and lower respiratory tract infections especially in infants and small children" (see Introduction). Given that the methods are well described in the prior art (see Johnson et al), there would have been a reasonable expectation of success in making the pharmaceutical composition comprising such antibodies or antigen-binding fragments. Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

CONCLUSION

In conclusion, all of the elements of the claims are known in the prior art. Further, as discussed above, there is motivation to combine all the prior art references to achieve what Applicant is claiming. Thus, no claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michelle Horning whose telephone number is 571-272-9036. The examiner can normally be reached on Monday-Friday, 8:30 am to 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 570-272-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for unpublished application is available through Private PAIR only. For more information about PAIR system, see htt://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Michelle Horning
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